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| Research Involving Children | Effective Date | |
| | Revisions Date | 7.1.2019 |

1.0 Purpose: This standard operating practice (SOP) establishes guidelines for the conduct and review of research involving children. This rule will address who can give consent for a child to participate in research, the assent process for informing the child participant and the rules by which the IRB uses to review and approve this type of research.

2.0 Research Protocols Affected:

- 2.1 Non-Exempt human research reviewed and approved by the University and Medical Center Institutional Review Board (UMCIRB) (both single site and multi-center).
- 2.2 Human research in which an ECU or ECU affiliate’s faculty, staff, or student serves on the research team.

3.0 SOP: This rule is to ensure investigators and other study team members as well as UMCIRB members are aware of requirements for conducting human research involving children. A child should be given the same consideration and respect when obtaining informed assent as is given to any other individual being asked to take part in research. However, this vulnerable class of individuals does require extra precautions and safeguards when developing applicable studies. Therefore, there are additional considerations that will be necessary in addition to the criteria for approval applied to all studies.

4.0 Definitions:

- 4.1 **Assent:** A child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.
- 4.2 **Children:** Persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.
- 4.3 **Emancipated Minor:** A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law, but who are entitled to treatment as if they had by virtue of assuming adult responsibilities, such as self-support, marriage, or procreation.
- 4.4 **Guardian:** An individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.
- 4.5 **Parent:** a child’s biological or adoptive parent.
- 4.6 **Permission:** The agreement of parent(s) or guardian to the participation of their child or ward in research.
- 4.7 **Reasonably Available:** Determining whether a parent is reasonably available to consent for those studies where both parents may be required to sign the parental consent involves assessing that parent’s location and the mechanism to secure consent. A parent may not be reasonably available when their whereabouts are unknown, their relationship with the child is such that the parent should not be contacted (i.e., in cases of domestic violence or other situations involving harm to the health or welfare of the child), the parent is incarcerated, on active military duty and not contactable, or the parent has chosen not to be involved the child’s care.
- 4.7 **Ward:** a child who is placed in the legal custody of the State or other agency, institution, or entity, consistent with applicable Federal, State, or local law.

5.0 Responsibilities:

5.1 UMCIRB/UMCIRB Chairperson or designee will

5.1.1. Take into account the ages, maturity, and psychological state of the children, either individually or as a group, as it deems appropriate to determine the appropriate format for obtaining and documenting assent in the intended study population or for individual subjects.

5.1.2 Ensure that research involving children falls into one of the following categories:

5.1.2.1 **Research involving no more than minimal risk.**

Adequate provisions must be made for soliciting assent of the children and permission of the parents or guardians.

5.1.2.2 **Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.**

The risk is justified by the anticipated benefit to the subjects; the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

5.1.2.3 **Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.**

The risk represents a minor increase over minimal risk; the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social or educational situations; the intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and adequate provisions are made for soliciting assent of the children and permission of their parents or guardians

5.1.2.4 **Research not otherwise approvable (under the three categories above) which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.)**

The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and the DHHS Secretary (or Commissioner of Food and Drugs, if FDA regulated), after consultation with experts in pertinent disciplines (for example: science, medicine, education, ethics, law), and following opportunity for public review and comment, has determined either (1) The research in fact satisfies the conditions of the categories above, or (2) the following conditions are met:

- The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.
- The research will be conducted in accordance with sound ethical principles.
- Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians

5.1.3 Review every assent process and document for the following:

- 5.3.1.6 On studies involving long-term follow-up, child participants will be consented for continuation of the study when they reach the age of majority. The consent process should be conducted no later than the first regularly scheduled visit after his/her birthday.
- 5.3.2 Consider the number of parental signatures required on the consent according to federal regulations, as follows:
 - 5.3.2.1 Research involving no greater than minimal risk requires one parent's signature.
 - 5.3.2.2 Research involving greater than minimal risk but presenting the prospect of direct benefit to the child requires one parent's signature.
 - 5.3.2.3 Research involving greater than minimal risk where there is no prospect of direct benefit to the child, but is likely to yield generalizable knowledge about the child's disorder or condition requires both parents' signatures, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
 - 5.3.2.4 Research not otherwise approvable but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children requires both parents' signatures, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
- 5.3.3 Contact the UMCIRB office for guidance regarding special exceptions or needs regarding the parental consent/child assent process.
- 5.3.4 Identify children as wards prior to enrollment or during the course of the research study. Principal investigators are responsible for notifying the UMCIRB prior to enrolling any child that is a ward into a research study. The principal investigator is responsible for notifying the UMCIRB regarding a child's status as a ward prior to initiating any research-related interventions if a child's status has changed from not being a ward to being a ward of the state.
 - 5.3.4.1 Children who are wards of the state or any other agency, institution or entity may participate in research, however, restrictions apply to the types of research where they may be enrolled. Children who are wards may only participate in research studies under section 5.1.2.3 and 5.1.2.4 above when at least one of the following conditions are met:
 - (1) The research study is about the child's status as a ward; or
 - (2) The research is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved are not wards.
 - 5.3.4.2 The UMCIRB requires that an advocate is appointed for each child that is a ward for research approved under section 5.1.2.3 and 5.1.2.4 above. The advocate serves in addition to any other individuals that might be acting on behalf of the child as a guardian or in loco parentis (in the place of a parent). The person serving as the child's advocate for participation in a research study must have the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research. An advocate may be assigned to one or more children. The advocate must not have a potential for conflict of interest, therefore, he/she must not be

- associated in any other way with the research study, the investigator, or the guardian institution. The advocate may be a member of the IRB.
- 5.3.5 Obtain IRB approval on all assent and consent processes and documents prior to commencing the enrollment of children.

6.0 Procedures:

- 6.1 Any research involving children requires their assent in one form or another, except when the IRB determines that:
- 6.1.1 The capability of the child to be involved in the assent process is limited because of age, state of consciousness, or other factors, or
- 6.1.2 The research holds out a prospect of direct benefit for the child that is not available with any of the current alternatives. In the latter case, the regulations recognize that parents/guardians and physicians control treatment choices and may properly override a child's refusal to take part in the research.
- 6.2 Parental/guardian permission should be obtained in accordance with general informed consent requirements, except when it is not a reasonable requirement in terms of protecting the children. An appropriate mechanism for protection needs to be described by the PI and needs to be consistent with federal, state and local laws (this exception to parent/guardian permission is not applicable in “more than minimal risk” FDA regulated research).
- 6.3 The permission of one or both parents or legal guardian is required based on the research risk and expected benefit or knowledge to be gained as outlined in section 5.3.2.
- 6.4 PI should submit applicable assent/parent permission/consent document with their IRB application.
- 6.5 The assent/parent permission/consent procedure will be pre-reviewed by UMCIRB staff to assess adherence to guidelines.
- 6.6 The assent/parent permission/consent procedure will be reviewed by the UMCIRB or UMCIRB Chair (or designee) within the context of the study.
- 6.6.1 Modifications to the procedures may be required before approval is granted.
- 6.7 PI and study team should use IRB approved assent/consent documents and adhere to approved plans for documentation.

Revision History:

| Date | Change | Reference Section(s) |
|----------|--|----------------------------|
| 7.1.2019 | Removed reference to regulations throughout document and placed one link in the reference section; updated office name to “UMCIRB office”; clarified PI responsibilities | Throughout and section 5.3 |

References

FDA. Code of Federal Regulations:
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50> and
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56>

DHHS, OHRP. Code of Federal Regulations:

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>

NC General Statute, Article 35, Emancipation:

http://www.ncga.state.nc.us/EnactedLegislation/Statutes/HTML/ByArticle/Chapter_7B/Article_35.html

DHHS, OHRP. SACHRP Recommendations, Parental Permission in Research involving Children, Focusing on “Not Reasonably Available”. October 17, 2018. <https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-d-november-13-2018/indes.html>